BLA Memorandum

***Subject*:** **Clinical Team Leader review memo regarding SGE patient representative**
From: **Peter Bross, Clinical Oncology Team Leader, OCTGT/CBER**
***To*:** **STN 125197 Sipuleucel-T/Provenge® BLA file**
Date: **April 26, 2010**

Background: PROVENGE® (Sipuleucel T, APC8015) is an autologous cellular immunotherapy product consisting of peripheral blood mononuclear cells (PBMCs) obtained from patients by leukapheresis and activated *in vitro* with a recombinant fusion protein (prostatic acid phosphatase fused with GM-CSF). A BLA was submitted, based on survival advantages observed in 2 randomized studies of asymptomatic or minimally symptomatic, metastatic, castrate resistant (hormone refractory) prostate cancer. Study 9902B enrolled 512 subjects: 341 subject in the sipuleucel-T arm and 171 subjects in the placebo arm. The primary analysis showed a statistically significant difference in overall survival favoring the sipuleucel-T arm; the difference in median survival times was 4.1 months (25.8 months vs. 21.7 months) in favor of sipuleucel-T. The safety of sipuleucel-T was evaluated in 904 patients randomized 2:1 in four blinded, placebo-controlled studies. Overall, treatment was relatively well tolerated: chills, fatigue, pyrexia, back pain, and nausea were the most common AEs. A possible increased risk of stroke was noted.

FDA has initiated a program of incorporating patient representative special government employees as advisors to FDA during the review process through the Office of Special Health Issues (OSHI) in the Office of the Commissioner. Mr. Jim Kiefert of Tucson, Arizona is an SGE for prostate cancer applications who was recommended by OSHI and cleared for receipt of confidential proprietary information. He was evaluated for of COI by the CBER Advisory Committee Executive Secretary and cleared for participation.

Mr. Kiefert was provided with the sponsor's study report and draft label and participated in 2 teleconferences with the clinical review team, on February 8, 2010 and again on April 25, 2010. Mr. Kiefert provided general advice regarding the indication statement, labeling, and patient instructions on the label and the clinical benefit noted in the study report. He indicated that he thought stroke was an important risk to patients. FDA will require the sponsor to complete a post marketing study to evaluate the risk of stroke in patients who receive sipuleucel-T.